

FILE 'USPAT' AT 16:19:35 ON 26 SEP 95

FILE 'USPAT' ENTERED AT 16:19:35 ON 26 SEP 95

=> s respiratory(w)syncial

11174 RESPIRATORY

0 SYNCIAL

L1 0 RESPIRATORY(W)SYNCIAL

=> s respiratory(w)syncial

11174 RESPIRATORY

13 SYNCIAL

L2 7 RESPIRATORY(W)SYNCIAL

=> d l2 1-7

1. 5,240,694, Aug. 31, 1993, Combined antiviral and antimediator treatment of common colds; Jack M. Gwaltney, Jr., 424/45, 405, 408, 434, 435, 451, 464, 489 [IMAGE AVAILABLE]

2. 5,104,854, Apr. 14, 1992, Antiviral peptides; Milton J. Schlesinger, et al., 514/15; 530/328 [IMAGE AVAILABLE]

3. 5,026,686, Jun. 25, 1991, Antiviral peptides; Milton J. Schlesinger, et al., 514/17, 8, 15, 16, 18; 530/322, 328, 329, 330; 930/220 [IMAGE AVAILABLE]

4. 4,920,209, Apr. 24, 1990, Oral vaccines; Alan R. Davis, et al., 435/235.1; 424/199.1, 227.1, 233.1; 435/69.3, 172.3 [IMAGE AVAILABLE]

5. 4,828,830, May 9, 1989, Method and composition for prophylaxis and treatment of viral infections; Grace H. W. Wong, 424/85.5, 85.1; 514/2 [IMAGE AVAILABLE]

6. 4,122,167, Oct. 24, 1978, \*\*Respiratory\*\* \*\*syncital\*\* vaccine; Eugene B. Buynak, et al., 424/211.1, 278.1; 435/237 [IMAGE AVAILABLE]

7. 3,919,044, Nov. 11, 1975, Processes for concentrating and purifying viruses and viral antigens; Joseph L. Melnick, et al., 435/239; 424/204.1, 209.1, 212.1, 213.1, 216.1, 217.1, 219.1, 229.1, 232.1; 435/272 [IMAGE AVAILABLE]

=> d l2 1-7 cit ab

1. 5,240,694, Aug. 31, 1993, Combined antiviral and antimediator treatment of common colds; Jack M. Gwaltney, Jr., 424/45, 405, 408, 434, 435, 451, 464, 489 [IMAGE AVAILABLE]

US PAT NO: 5,240,694 [IMAGE AVAILABLE]

L2: 1 of 7

ABSTRACT:

The common cold is best treated by providing a combination of antiviral agents and antiinflammatory compounds to a patient infected with a cold virus. An antiviral agent and two antiinflammatory compounds given to a person infected with a cold virus simultaneously reduces the likelihood of a cold developing and the amount and duration of viral shedding, as well as substantially reduces the severity of individual cold symptoms and the overall number and severity of cold symptoms. Supplementing the activity of the combined antiviral and antiinflammatory agents with such compounds as antihistamines and alpha agonists results in surprisingly good nasal benefits. The combination therapy, termed COVAM therapy, is well tolerated and has no evidence of short-term toxicity.

2. 5,104,854, Apr. 14, 1992, Antiviral peptides; Milton J. Schlesinger, et al., 514/15; 530/328 [IMAGE AVAILABLE]

US PAT NO: 5,104,854 [IMAGE AVAILABLE]

L2: 2 of 7

**ABSTRACT:**

Novel antiviral peptides are disclosed which have a sequence of about 6 to 30 amino acids and which are substantially identical to a small portion of a glycoprotein in a virus that contains a lipid-bilayer in its structure. A preferred peptide having antiviral activity against influenza virus is the decapeptide amide N-G-S-L-Q-C-R-I-C-I-NH<sub>2</sub> [SEQ ID NO:3].

3. 5,026,686, Jun. 25, 1991, Antiviral peptides; Milton J. Schlesinger, et al., 514/17, 8, 15, 16, 18; 530/322, 328, 329, 330; 930/220 [IMAGE AVAILABLE]

US PAT NO: 5,026,686 [IMAGE AVAILABLE]

L2: 3 of 7

**ABSTRACT:**

Novel antiviral peptides are disclosed which have a sequence of about 4 to 10 amino acids and which are substantially identical to a small portion of the cytoplasmic domain of a glycoprotein in a virus that contains a lipid-bilayer in its structure.

4. 4,920,209, Apr. 24, 1990, Oral vaccines; Alan R. Davis, et al., 435/235.1; 424/199.1, 227.1, 233.1; 435/69.3, 172.3 [IMAGE AVAILABLE]

US PAT NO: 4,920,209 [IMAGE AVAILABLE]

L2: 4 of 7

**ABSTRACT:**

Methods and vaccines for the production of antibodies to infectious organisms are described. Live recombinant adenovirus containing a foreign gene coding for an antigen produced by another infectious organism is delivered to the intestine of a warm-blooded animal in an enteric-coated dosage form, whereupon the virus infects the gut wall and induces the production of antibodies or cell mediated immunity to both adenovirus and the other infectious organism.

5. 4,828,830, May 9, 1989, Method and composition for prophylaxis and treatment of viral infections; Grace H. W. Wong, 424/85.5, 85.1; 514/2 [IMAGE AVAILABLE]

US PAT NO: 4,828,830 [IMAGE AVAILABLE]

L2: 5 of 7

**ABSTRACT:**

TNF or LT qualitatively and quantitatively potentiates the anti-viral activity of interferons, thus permitting the use of lower interferon doses to protect uninfected cells from interferon sensitive and relatively insensitive viruses and to selectively kill virus-infected cells.

6. 4,122,167, Oct. 24, 1978, \*\*Respiratory\*\* \*\*syncytial\*\* vaccine; Eugene B. Buynak, et al., 424/211.1, 278.1; 435/237 [IMAGE AVAILABLE]

US PAT NO: 4,122,167 [IMAGE AVAILABLE]

L2: 6 of 7

**ABSTRACT:**

By serially passaging virulent respiratory syncytial virus in human diploid lung fibroblasts, a non-pathogenic but antigenic live respiratory syncytial virus is produced. This virus is useful in preparing a live virus vaccine.

7. 3,919,044, Nov. 11, 1975, Processes for concentrating and purifying viruses and viral antigens; Joseph L. Melnick, et al., 435/239; 424/204.1, 209.1, 212.1, 213.1, 216.1, 217.1, 219.1, 229.1, 232.1; 435/272 [IMAGE AVAILABLE]

US PAT NO: 3,919,044 [IMAGE AVAILABLE]

L2: 7 of 7

**ABSTRACT:**

Viruses and viral antigens harvested from embryonated eggs or tissue culture, whether acid-sensitive or acid-resistant, are purified and concentrated by processes which substantially eliminate the nonviral proteins present in the virus stock and thereafter permit the collection of a solute containing substantially all of the virus and viral antigens which were present in the starting stock. For both acid-resistant and acid-sensitive viruses the processes of the invention comprise the elimination of nonviral protein by filtration or batch adsorption with resins discovered to selectively adsorb certain nonviral proteins. In the case of acid-sensitive viruses, the viruses are stabilized against subsequent acidification by the treatment of the resulting filtrate with a salt selected from

the group consisting of ammonium sulfate, sodium sulfate, ammonium chloride and magnesium sulfate to complete the removal of nonviral protein. In both cases the viruses and viral antigens are acidified to pH 3-6 and adsorbed on preselected reactive materials from which the purified and concentrated virus is selectively extracted by elution with an eluent of pH 10-12 or higher which does not impair viral activity.

=> s respiratory(w)syncytial  
11174 RESPIRATORY  
366 SYNCYTIAL  
L3 289 RESPIRATORY(W)SYNCYTIAL

=> s l3 and propiolactone  
1195 PROPIOLACTONE  
L4 5 L3 AND PROPIOLACTONE

=> d l4 1-4 cit kwic

1. 5,200,179, Apr. 6, 1993, Vaccine; Dale Bordt, et al., 424/202.1, 204.1, 211.1, 218.1, 221.1, 223.1, 229.1, 233.1, 234.1, 278.1 [IMAGE AVAILABLE]

US PAT NO: 5,200,179 [IMAGE AVAILABLE] L4: 1 of 5  
SUMMARY:

BSUM(3)

A number of methods are known for inactivating viruses or bacteria, such as treatment with .beta.-\*\*propiolactone\*\*, formaldehyde or ethyleneimine. Such reagents are, however, potentially hazardous to handle and safer techniques are desirable.

SUMMARY:

BSUM(11)

The advantage of the invention is that carcinogenic or otherwise hazardous reagents known in the art for viral inactivation, such as .beta.-\*\*propiolactone\*\*, formaldehyde and ethyleneimine, are no longer required, thereby making the inactivation procedure safer.

DETDESC:

DETD(50)

Inactivation of Bovine \*\*Respiratory\*\* \*\*Syncytial\*\* Virus (BRSV)  
CLAIMS:

CLMS(2)

2. . . . consisting of transmissible gastroenteritis virus of swine, parvovirus, members of the Herpes virus group, paramyxo, parainfluenza-3, bovine coronavirus, and bovine \*\*respiratory\*\* \*\*syncytial\*\* virus.  
2. 5,166,057, Nov. 24, 1992, Recombinant negative strand RNA virus expression-systems; Peter Palese, et al., 435/69.1, 172.3, 194, 235.1, 320.1; 935/32, 34, 57 [IMAGE AVAILABLE]

US PAT NO: 5,166,057 [IMAGE AVAILABLE] L4: 2 of 5  
DETDESC:

DETD(8)

The . . . negative strand RNA virus templates and chimeric viruses including, but not limited to paramyxoviruses, such as parainfluenza viruses, measles viruses, \*\*respiratory\*\* \*\*syncytial\*\* virus; bunyaviruses; arena viruses; etc. A particularly interesting virus system that can be used in accordance with the invention are. . .  
DETDESC:

DETD(55)

In . . . grown in cell culture or in the allantois of the chick embryo, purified by zonal ultracentrifugation, inactivated by formaldehyde or .beta.-\*\*propiolactone\*\*, and pooled. The resulting vaccine is usually inoculated intramuscularly.

3. 5,069,901, Dec. 3, 1991, Preparation of a recombinant subunit vaccine against pseudorabies infection; Elaine V. Jones, et al., 424/199.1, 223.1, 229.1, 278.1, 283.1; 435/5, 172.3, 235.1, 238, 320.1; 530/826; 935/59, 63 [IMAGE AVAILABLE]

US PAT NO: 5,069,901 [IMAGE AVAILABLE] L4: 3 of 5  
SUMMARY:

BSUM(14)

Recently, . . . (Wiktor, et al., Proc. Natl. Acad. Sci. USA 81:7194(1984)), vesicular stomatitis glycoprotein G (Mackett, et al., Science 227:433(1985), and human \*\*respiratory\*\* \*\*syncytial\*\* virus G glycoprotein (Ball, et al., Proc. Natl. Acad. Sci. USA 83:246(1986); Elango, et al., Proc. Natl. Acad. Sci. USA. . .

DETDESC:

DETD(113)

Culture . . . for production of bacterins are grown to an optical density (OD) of 1-3 units and then inactivated by adding beta \*\*propiolactone\*\* (BPL) to a final concentration of 0.2%. The cultures are then agitated 12 hours at 20.degree. C. and fixed with. . .

4. 4,965,069, Oct. 23, 1990, Oxidized viruses or viral antigens and utilization for diagnostic prophylactic and/or therapeutic applications; Gerard A. Quash, et al., 424/208.1, 204.1, 209.1, 211.1, 212.1, 215.1, 216.1, 219.1, 225.1, 230.1, 231.1; 435/238 [IMAGE AVAILABLE]

US PAT NO: 4,965,069 [IMAGE AVAILABLE] L4: 4 of 5  
DRAWING DESC:

DRWD(3)

FIG. . . . administration of untreated parainfluenza virus (PIV) virus (A; control); PIV having an oxidized oligosaccharide moiety (B); PIV conventionally inactivated using beta-\*\*propiolactone\*\* (C); and PIV conventionally inactivated using beta-\*\*propiolactone\*\* and having an oxidized oligosaccharide moiety (D). Antibody titers were evaluated following 2 intraperitoneal injections of each of the PIV. . .

DETDESC:

DETD(41)

Specific . . . etc.; Parvoviridae such as parvoviruses, etc.; RNA viruses such as Togaviridae such as rubella, etc.; Paramyxoviridae such as measles, parainfluenza, \*\*respiratory\*\* \*\*syncytial\*\* virus, etc.; Flaviviridae such as dengue virus types 1-4, yellow fever virus, tick-borne fever viruses, etc.; Rhabdoviridae such as rabies, . . .

DETDESC:

DETD(92)

Infectivity of PIV inactivated by a conventional method using beta-\*\*propiolactone\*\* was also determined for comparison. Beta-\*\*propiolactone\*\* (Fluka) was added (final concentration 0.05% v/v) to purified PIV (2 mg protein/ml) in 100 mM sodium borate-HCl, pH 9.0, and the mixture incubated for 2 hours 37.degree. C. At that time, fresh beta-\*\*propiolactone\*\* was added (final concentration 0.05% v/v) and the mixture incubated for an additional 2 hours. The virus was then dialysed. . .

DETDESC:

DETD(93)

Another sample of purified PIV was first conventionally inactivated using beta-\*\*propiolactone\*\* and then the oligosaccharide moiety oxidized as described above. The inactivated oxidized PIV was then extensively dialysed against PBS at. . .

DETDESC:

DETD(99)

As . . . the virus. In fact, oxidation of the carbohydrate moiety of the PIV virion was as effective as conventional inactivation using beta-\*\*propiolactone\*\*.

DETDESC:

DETD(102)

Sixty-six . . . groups: Group 1 (control) untreated PIV; Group 2, PIV having an oxidized oligosaccharide moiety; Group 3, PIV conventionally inactivated using beta-\*\*propiolactone\*\*; and Group 4, PIV conventionally inactivated using beta-\*\*propiolactone\*\* and having an oxidized oligosaccharide moiety. Animals in Series A, Series B and Series C received respectively-one (on day 0). . .

DETDESC:

DETD(109)

From . . . antibody response when administered in vivo. This response occurred earlier than that elicited by PIV inactivated by conventional methods using beta-\*\*propiolactone\*\*.

=> s l3 and octyl(w)glucopyranoside  
40745 OCTYL  
682 GLUCOPYRANOSIDE  
6 OCTYL(W)GLUCOPYRANOSIDE  
L5 2 L3 AND OCTYL(W)GLUCOPYRANOSIDE

=> d l5 1-2 kwic

US PAT NO: 4,871,488 [IMAGE AVAILABLE]

L5: 1 of 2

SUMMARY:

BSUM(8)

The . . . agglutinate and lyse red blood cells. In a preferred aspect, the method of the invention utilizes the nonionic detergent .beta.-D- \*\*octyl\*\*-\*\*glucopyranoside\*\*, which is rapidly and easily removed as the means

of extracting the membrane proteins from the viral particles. This procedure. . .

SUMMARY:

BSUM(11)

In . . . nonionic detergents containing sugar head groups such as the alkyl glucosides. A particularly preferred nonionic detergent for this purpose is .beta.-D-\*\*octyl\*\*-\*\*glucopyranoside\*\*. Utilization of this method allows efficient reconstitution of the membrane proteins into the liposomes with retention of biological activities. This. . .

SUMMARY:

BSUM(14)

Suitable . . . the method of the invention include Sendai, influenza, herpes simplex or genitalis, HTLV I, II or III, retroviruses, pox virus, \*\*respiratory\*\* \*\*syncytial\*\* virus, toga virus, and the like. The present invention can also be employed in conjunction with membrane proteins derived from. . .

US PAT NO: 4,663,161 [IMAGE AVAILABLE] L5: 2 of 2

SUMMARY:

BSUM(8)

The . . . agglutinate and lyse red blood cells. In a preferred aspect, the method of the invention utilizes the nonionic detergent .beta.-D- \*\*octyl\*\*-\*\*glucopyranoside\*\*, which is rapidly and easily removed as the means of extracting the membrane proteins from the viral particles. This procedure. . .

SUMMARY:

BSUM(11)

In . . . nonionic detergents containing sugar head groups such as the alkyl glucosides. A particularly preferred nonionic detergent for this purpose is .beta.-D-\*\*octyl\*\*-\*\*glucopyranoside\*\*. Utilization of this method allows efficient reconstitution of the membrane proteins into the liposomes with retention of biological activities. This. . .

SUMMARY:

BSUM(14)

Suitable . . . the method of the invention include Sendai, influenza, herpes simplex or genitalis, HTLV I, II or III, retroviruses, pox virus, \*\*respiratory\*\* \*\*syncytial\*\* virus, toga virus, rhabdovire bunyavise, and the like. The present invention can also be employed in conjunction with membrane proteins. . .

=> d 15 1-2 cit ab

1. 4,871,488, Oct. 3, 1989, Reconstituting viral glycoproteins into large phospholipid vesicles; Raphael J. Mannino, et al., 264/4.6, 4.3; 424/1.21, 450; 428/402.2; 436/829; 514/8, 885 [IMAGE AVAILABLE]

US PAT NO: 4,871,488 [IMAGE AVAILABLE] L5: 1 of 2

ABSTRACT:

The present disclosure relates to novel liposome compositions and methods for their preparation. Utilization of the present invention provides an efficient reconstitution of membrane proteins into large (0.1 to 2 micron diameter) phospholipid vesicles with a large, internal aqueous space. The method has been exemplified with the use of glycoproteins of influenza (A/PR8/34) and Sendai (parainfluenza type I) viruses. The method comprises (A) extracting out the desired membrane protein from a source biological material with an extraction buffer

comprising a detergent; (B) mixing the extract with a phospholipid solution and deriving a cochleate intermediate; and (C) forming large phospholipid vesicles with integrated membrane protein in a biologically active state.

2. 4,663,161, May 5, 1987, Liposome methods and compositions; Raphael J. Mannino, et al., 424/450; 264/4.6; 424/204.1, 209.1, 211.1, 812; 428/402.2; 436/829 [IMAGE AVAILABLE]

US PAT NO: 4,663,161 [IMAGE AVAILABLE] L5: 2 of 2

**ABSTRACT:**

The present disclosure relates to novel liposome compositions and methods for their preparation. Utilization of the present invention provides an efficient reconstitution of membrane proteins into large (0.1 to 2 micron diameter) phospholipid vesicles with a large, internal aqueous space. The method has been exemplified with the use of glycoproteins of influenza (A/PR8/34) and Sendai (parainfluenza type I) viruses.

=> s l3 and glucopyranoside

682 GLUCOPYRANOSIDE

L6 9 L3 AND GLUCOPYRANOSIDE

=> d l6 1-9 cit kwic

1. 5,177,064, Jan. 5, 1993, Targeted drug delivery via phosphonate derivatives; Nicholas S. Bodor, 514/51, 49, 50, 885; 536/6.4, 17.1, 17.5, 18.7; 552/502; 558/70 [IMAGE AVAILABLE]

US PAT NO: 5,177,064 [IMAGE AVAILABLE] L6: 1 of 9

**SUMMARY:**

BSUM(11)

Ribavirin is active against several influenza viruses and \*\*respiratory\*\* \*\*syncytial\*\* virus and as such is used in an aerosol form to treat these diseases. Ribavirin is also used in the. . .

**DETDESC:**

DETD(75)

Among . . . a 5'-hydroxyl. Non-nucleoside antivirals for possible derivatization herein include hydroxy-containing glycosides such as 2-deoxy-D-glucose and 2-deoxy-2-fluoro-D-mannose, phenyl glucosides such as phenyl-6-chloro-6-deoxy-.beta.-D-\*\*glucopyranoside\*\* and benzimidazole analog type antivirals such as the syn and anti isomers of 6[(hydroxyimino)phenyl]methyl]-1-[(1-methylethyl)sulfonyl]-1H-benzimidazol-2-amine.

2. 4,871,488, Oct. 3, 1989, Reconstituting viral glycoproteins into large phospholipid vesicles; Raphael J. Mannino, et al., 264/4.6, 4.3; 424/1.21, 450; 428/402.2; 436/829; 514/8, 885 [IMAGE AVAILABLE]

US PAT NO: 4,871,488 [IMAGE AVAILABLE] L6: 2 of 9

**SUMMARY:**

BSUM(8)

The . . . agglutinate and lyse red blood cells. In a preferred aspect, the method of the invention utilizes the nonionic detergent .beta.-D- octyl-\*\*glucopyranoside\*\*, which is rapidly and easily removed as the means of extracting the membrane proteins from the viral particles. This procedure. . .

**SUMMARY:**

BSUM(11)

In . . . nonionic detergents containing sugar head groups such as the alkyl glucosides. A particularly preferred nonionic detergent for this purpose is .beta.-D-octyl-\*\*glucopyranoside\*\*. Utilization of this method allows efficient reconstitution of the membrane proteins into the liposomes with retention of biological activities. This. . .

SUMMARY:

BSUM(14)

Suitable . . . the method of the invention include Sendai, influenza, herpes simplex or genitalis, HTLV I, II or III, retroviruses, pox virus, \*\*respiratory\*\* \*\*syncytial\*\* virus, toga virus, and the like. The present invention can also be employed in conjunction with membrane proteins derived from. . .

DETDESC:

DETD(3)

Materials. . . Avanti Polar Lipids, Birmingham, Ala in glass ampules and stored under nitrogen at -20.degree. C. Cholesterol (porcine liver) grade I, n-octyl-.beta.-D-\*\*glucopyranoside\*\*, fluorescein isothiocyanate (FITC)-dextran (average mol. wt. 67,000), metrizamide grade I, and chemicals for buffers and protein and phosphate determinations, were. . .

3. 4,663,161, May 5, 1987, Liposome methods and compositions; Raphael J. Mannino, et al., 424/450; 264/4.6; 424/204.1, 209.1, 211.1, 812; 428/402.2; 436/829 [IMAGE AVAILABLE]

US PAT NO: 4,663,161 [IMAGE AVAILABLE]

L6: 3 of 9

SUMMARY:

BSUM(8)

The . . . agglutinate and lyse red blood cells. In a preferred aspect, the method of the invention utilizes the nonionic detergent .beta.-D- octyl-\*\*glucopyranoside\*\*, which is rapidly and easily removed as the means of extracting the membrane proteins from the viral particles. This procedure. . .

SUMMARY:

BSUM(11)

In . . . nonionic detergents containing sugar head groups such as the alkyl glucosides. A particularly preferred nonionic detergent for this purpose is .beta.-D-octyl-\*\*glucopyranoside\*\*. Utilization of this method allows efficient reconstitution of the membrane proteins into the liposomes with retention of biological activities. This. . .

SUMMARY:

BSUM(14)

Suitable . . . the method of the invention include Sendai, influenza, herpes simplex or genitalis, HTLV I, II or III, retroviruses, pox virus, \*\*respiratory\*\* \*\*syncytial\*\* virus, toga virus, rhabdovire bunyavise, and the like. The present invention can also be employed in conjunction with membrane proteins. . .

DETDESC:

DETD(4)

Materials. . . Avanti Polar Lipids, Birmingham, Ala in glass ampules and stored under nitrogen at -20.degree. C. Cholesterol (porcine liver) grade I, n-octyl-.beta.-D-\*\*glucopyranoside\*\*, fluorescein isothiocyanate (FITC)-dextran (average mol. wt. 67,000), metrizamide grade I, and chemicals for buffers and protein and phosphate determinations, were. . .

4. 4,574,058, Mar. 4, 1986, Antigen derivatives and processes for their preparation; Gerhard Baschang, et al., 536/17.2; 260/998.2; 530/322, 807; 536/17.3 [IMAGE AVAILABLE]

US PAT NO: 4,574,058 [IMAGE AVAILABLE]

L6: 4 of 9

SUMMARY:

B

=> s l3 and (ascorbic(w)acid or ascorbate)  
15298 ASCORBIC  
363117 ACID

12581 ASCORBIC(W)ACID  
3202 ASCORBATE

L7 24 L3 AND (ASCORBIC(W)ACID OR ASCORBATE)

=> d l7 1-24

1. 5,370,994, Dec. 6, 1994, Solid phase assay for urea; Thomas N. Stewart, et al., 435/12; 422/56, 57; 435/7.91, 805, 970; 436/904 [IMAGE AVAILABLE]

2. 5,328,831, Jul. 12, 1994, Substrate composition for solid phase urease immunoassay; Thomas N. Stewart, et al., 435/12, 7.91, 188; 436/904 [IMAGE AVAILABLE]

3. 5,212,050, May 18, 1993, Method of forming a permselective layer; Randall M. Mier, et al., 430/320, 311, 313, 325, 326, 328, 330; 435/288 [IMAGE AVAILABLE]

4. 5,200,179, Apr. 6, 1993, Vaccine; Dale Bordt, et al., 424/202.1, 204.1, 211.1, 218.1, 221.1, 223.1, 229.1, 233.1, 234.1, 278.1 [IMAGE AVAILABLE]

5. 5,200,051, Apr. 6, 1993, Wholly microfabricated biosensors and process for the manufacture and use thereof; Stephen N. Cozzette, et al., 204/403, 153.12, 153.17, 415; 435/288, 291 [IMAGE AVAILABLE]

6. 5,139,934, Aug. 18, 1992, Substrate composition and method for solid phase urease immunoassay; Thomas N. Stewart, et al., 435/7.92, 7.93, 7.94, 7.95, 12, 970; 436/518, 527, 528, 529, 530, 810, 904 [IMAGE AVAILABLE]

7. 5,063,081, Nov. 5, 1991, Method of manufacturing a plurality of uniform microfabricated sensing devices having an immobilized ligand receptor; Stephen N. Cozzette, et al., 435/4; 204/153.12, 403, 415, 418; 422/57; 427/2.13, 407.1, 414; 435/7.1 [IMAGE AVAILABLE]

8. 4,810,631, Mar. 7, 1989, Signal enhancement in immunoassay by modulation of chemical catalysis; Michael E. Perlman, et al., 435/7.1, 7.9, 7.91, 7.94, 18, 19, 21, 810, 966; 436/518, 537, 808, 821 [IMAGE AVAILABLE]

9. 4,391,904, Jul. 5, 1983, Test strip kits in immunoassays and compositions therein; David J. Litman, et al., 435/7.91; 422/55, 56; 435/188, 805, 975; 436/536, 537 [IMAGE AVAILABLE]

10. 4,374,925, Feb. 22, 1983, Macromolecular environment control in specific receptor assays; David J. Litman, et al., 435/7.91, 5, 7.31, 7.32, 7.33, 7.34, 7.35, 7.36, 7.37, 7.8, 7.92, 177, 810, 966, 968, 971; 436/529, 800 [IMAGE AVAILABLE]

11. 4,366,241, Dec. 28, 1982, Concentrating zone method in heterogeneous immunoassays; Henry K. Tom, et al., 435/7.91; 422/56; 435/5, 7.9, 7.92, 805, 810, 968, 975; 436/541, 800, 807 [IMAGE AVAILABLE]
12. 4,355,021, Oct. 19, 1982, Virucidal wipe and method; Mearl C. Mahl, et al., 424/443, 667 [IMAGE AVAILABLE]
13. 4,328,311, May 4, 1982, Enzyme-aminoglycoside conjugates; Gerald L. Rowley, et al., 435/188, 177; 530/345, 375, 391.9, 405, 406, 408, 806 [IMAGE AVAILABLE]
14. 4,287,300, Sep. 1, 1981, Charge effects in enzyme immunoassays; Ian Gibbons, et al., 435/5, 7.32, 7.9, 188, 810; 436/527, 529, 531, 546, 547, 800, 805, 806, 811, 815, 820 [IMAGE AVAILABLE]
15. 4,281,061, Jul. 28, 1981, Double antibody for enhanced sensitivity in immunoassay; Robert F. Zuk, et al., 435/7.9, 5, 7.2, 7.31, 7.32, 7.33, 7.34, 7.35, 7.36, 7.37, 7.7, 7.8, 7.91, 188, 966, 968, 971; 436/537, 540, 800, 808 [IMAGE AVAILABLE]
16. 4,275,149, Jun. 23, 1981, Macromolecular environment control in specific receptor assays; David J. Litman, et al., 435/7.91, 5, 6, 7.1, 7.2, 7.31, 7.32, 7.33, 7.34, 7.35, 7.36, 7.37, 7.71, 7.72, 7.8, 7.92, 177, 178, 810, 968, 971; 436/531 [IMAGE AVAILABLE]
17. 4,235,869, Nov. 25, 1980, Assay employing a labeled Fab-fragment ligand complex; Moshe Schwarzberg, 436/512; 250/302; 435/7.7, 7.72, 968; 436/513, 536, 537, 541, 800 [IMAGE AVAILABLE]
18. 4,233,402, Nov. 11, 1980, Reagents and method employing channeling; Edward T. Maggio, et al., 435/5, 7.7, 7.91, 968; 436/537, 805 [IMAGE AVAILABLE]
19. 4,233,401, Nov. 11, 1980, Antienzyme homogeneous competitive binding assay; Robert A. Yoshida, et al., 435/7.8, 7.9, 185, 810, 963 [IMAGE AVAILABLE]
20. 4,224,413, Sep. 23, 1980, Cell culture method; Colin Burbidge, 435/284, 285, 313, 812 [IMAGE AVAILABLE]
21. 4,220,722, Sep. 2, 1980, Method for conjugating to polyamino compounds employing haloacyl groups and compositions prepared thereby; Gerald L. Rowley, et al., 435/188, 7.9, 177, 961, 964; 436/537, 816, 823; 530/322, 345, 395, 403, 404, 405, 406, 408, 409, 410, 806 [IMAGE AVAILABLE]
22. 4,208,479, Jun. 17, 1980, Label modified immunoassays; Robert F. Zuk, et al., 435/7.9, 7.72, 7.8; 436/512, 537, 808, 826 [IMAGE AVAILABLE]
23. 4,160,645, Jul. 10, 1979, Catalyst mediated competitive protein binding assay; Edwin F. Ullman, 436/517, 537, 803, 805, 806, 816 [IMAGE AVAILABLE]
24. 4,144,126, Mar. 13, 1979, Cell culture method; Colin Burbidge, 435/235.1, 240.24, 811 [IMAGE AVAILABLE]

= > s 14 and inactiv?

64956 INACTIV?

L8 5 L4 AND INACTIV?

= > d 18 1-5 cit kwic

1. 5,200,179, Apr. 6, 1993, Vaccine; Dale Bordt, et al., 424/202.1, 204.1, 211.1, 218.1, 221.1, 223.1, 229.1, 233.1, 234.1, 278.1 [IMAGE AVAILABLE]

presence of oxygen and a source. . .

CLAIMS:

CLMS(2)

2. . . . consisting of transmissible gastroenteritis virus of swine, parvovirus, members of the Herpes virus group, paramyxo, parainfluenza-3, bovine coronavirus, and bovine \*\*respiratory\*\* \*\*syncytial\*\* virus.

CLAIMS:

CLMS(4)

4. A vaccine according to claim 1 which comprises a prophylactically effective amount of an \*\*inactivated\*\* bacterium and is an \*\*inactivated\*\* vaccine against bacteria.

CLAIMS:

CLMS(7)

7. A vaccine according to claim 1 in which the live virus or bacterium was \*\*inactivated\*\* in a medium additionally comprising saponin.

CLAIMS:

CLMS(8)

8. A vaccine according to claim 1 in which the live virus or bacterium was \*\*inactivated\*\* in the presence of a stabilizing agent capable of enhancing antigen stability.

CLAIMS:

CLMS(10)

10. A process for preparing a vaccine, which process comprises admixing an \*\*inactivated\*\* virus or bacterium with a pharmaceutically acceptable carrier, wherein the \*\*inactivated\*\* virus or bacterium was prepared by \*\*inactivating\*\* a live virus or bacterium with ascorbic acid and/or a salt thereof in the presence of oxygen and a source. . .

CLAIMS:

CLMS(11)

11. A process for preparing a vaccine including an \*\*inactivated\*\* virus or bacterium which composition is substantially free from live viruses or bacteria, which process comprises \*\*inactivating\*\* a live virus or bacterium with ascorbic acid and/or a salt thereof in the presence of oxygen and a source. . .

CLAIMS:

CLMS(13)

13. A method according to claim 12 in which the vaccine comprises an \*\*inactivated\*\* virus.

2. 5,166,057, Nov. 24, 1992, Recombinant negative strand RNA virus expression-systems; Peter Palese, et al., 435/69.1, 172.3, 194, 235.1, 320.1; 935/32, 34, 57 [IMAGE AVAILABLE]

DETDESC:

DETD(8)

The . . . negative strand RNA virus templates and chimeric viruses including, but not limited to paramyxoviruses, such as parainfluenza viruses, measles viruses, \*\*respiratory\*\* \*\*syncytial\*\* virus; bunyaviruses; arena viruses; etc. A particularly interesting virus system that can be used in accordance with the invention are. . .

DETDESC:

DETD(52)

Either a live recombinant viral vaccine or an \*\*inactivated\*\* recombinant viral vaccine can be formulated. A live vaccine may be preferred because multiplication in the host leads to a. . .

DETDESC:

DETD(54)

Alternatively, . . . to induce an immune response. Alternatively, larger quantities of the strains could be administered, so that these preparations serve as \*\*inactivated\*\* (killed) virus, vaccines. For \*\*inactivated\*\* vaccines, it is preferred that the heterologous gene product be expressed as a viral component, so that the gene product. . . is associated with the virion. The advantage of such preparations is that they contain native proteins and do not undergo \*\*inactivation\*\* by treatment with formalin or other agents used in the manufacturing of killed virus vaccines.

DETDESC:

DETD(55)

In another embodiment of this aspect of the invention, \*\*inactivated\*\* vaccine formulations may be prepared using conventional techniques to "kill" the chimeric viruses. \*\*Inactivated\*\* vaccines are "dead" in the sense that their infectivity has been destroyed. Ideally, the infectivity of the virus is destroyed without affecting its immunogenicity. In order to prepare \*\*inactivated\*\* vaccines, the chimeric virus may be grown in cell culture or in the allantois of the chick embryo, purified by zonal ultracentrifugation, \*\*inactivated\*\* by formaldehyde or .beta.-\*\*propiolactone\*\*, and pooled. The resulting vaccine is usually inoculated intramuscularly.

DETDESC:

DETD(56)

\*\*Inactivated\*\* viruses may be formulated with a suitable adjuvant in order to enhance the immunological response. Such adjuvants may include but. . .

DETDESC:

DETD(82)

In . . . specific transcription product seen (FIG. 3A, lane 3). Additional experiments showed globin mRNA, containing a terminal cap 1 structure, was \*\*inactive\*\* as primer using initial preparations of polymerase.

3. 5,069,901, Dec. 3, 1991, Preparation of a recombinant subunit vaccine against pseudorabies infection; Elaine V. Jones, et al., 424/199.1, 223.1, 229.1, 278.1, 283.1; 435/5, 172.3, 235.1, 238, 320.1; 530/826;

935/59, 63 [IMAGE AVAILABLE]

US PAT NO: 5,069,901 [IMAGE AVAILABLE]

L8: 3 of 5

**ABSTRACT:**

A method of preparation of a vaccine for use in immunizing animals against pseudorabies virus (PRV) infection which comprises \*\*inactivated\*\* recombinant PRV subunit antigens. Also described is a diagnostic kit for detection of PRV infection which distinguishes vaccinated animals from. . .

**SUMMARY:**

BSUM(2)

This invention relates to a method of preparation of an \*\*inactivated\*\* subunit vaccine useful for the immunization of animals against the pseudorabies virus (PRV) and the development of a diagnostic test. . .

**SUMMARY:**

BSUM(5)

The . . . (Gustafson, in Diseases of Swine, Dunn and Ledman, Eds., Iowa State Press, 1975). Current control measures include vaccination with either \*\*inactivated\*\* or attenuated PRV or test and removal procedures (See Gustafson, *supra*, (1975)).

**SUMMARY:**

BSUM(6)

Modified live virus (MLV) and \*\*inactivated\*\* whole virus vaccines have been used extensively as a source to induce immunity against many diseases. Modified live virus stocks. . .

**SUMMARY:**

BSUM(7)

PRV . . . the environment. Thus, complete eradication of the virus is impossible. An alternative vaccination approach would be the use of an \*\*inactivated\*\* recombinant vaccine expressing selected immunogenic PRV glycoproteins. The development of such a vaccine requires a knowledge of the organization of. . .

**SUMMARY:**

BSUM(14)

Recently, . . . (Wiktor, et al., Proc. Natl. Acad. Sci. USA 81:7194(1984)), vesicular stomatitis glycoprotein G (Mackett, et al., Science 227:433(1985), and human \*\*respiratory\*\* \*\*syncytial\*\* virus G glycoprotein (Ball, et al., Proc. Natl. Acad. Sci., USA 83:246(1986); Elango, et al., Proc. Natl. Acad. Sci. USA. . .

**SUMMARY:**

BSUM(17)

In . . . comprises expressing PRV subunit antigens, gp50:63 in a vaccinia virus tissue culture system; treating the recombinant virus with a chemical \*\*inactivating\*\* agent and collecting the \*\*inactivated\*\* recombinant virus and cell extract for formulation into a vaccine.

**SUMMARY:**

BSUM(19)

In . . . a recombinant vaccinia virus which expresses the PRV gp50:63 is described wherein the recombinant vaccinia and cell extract has been \*\*inactivated\*\*.

DETDESC:

DETD(3)

In one embodiment of the invention, a method of preparation of a recombinant \*\*inactivated\*\* subunit vaccine or derivatives thereof for pseudorabies infection is set forth. The PRV subunit vaccine is constructed so as to. . .

DETDESC:

DETD(12)

A . . . the invention does not contain gI protein or DNA sequence it can also be used in similar assays. For example, \*\*inactivated\*\* recombinant vaccinia virus containing PRV gp50 and gp63 is not infectious and cannot initiate an immune response to PRV proteins. . .

DETDESC:

DETD(21)

An \*\*inactivated\*\* subunit vaccine produced by the expression of gp50:gp63 using the vaccinia vector system can be used to successfully immunize animals against PRV infection. The vaccine produced using this method contains no intact PRV, i.e., no attenuated or \*\*inactivated\*\* PRV is present.

DETDESC:

DETD(22)

Using . . . as the subunit component, the subunit vaccine has been demonstrated to induce a strong protective immunity when administered as an \*\*inactivated\*\* preparation containing the gp50:63 antigens in a recombinant vaccinia virus preparation in the presence of host cell extract.

DETDESC:

DETD(23)

Tests . . . live recombinant is least virulent and most protective when the mice are inoculated intracranially. Use of recombinant gp50:63 (Vgp50:63) preparations \*\*inactivated\*\* with a solution of binary ethylene imine (BEI) are safer and less expensive than currently available vaccines since vaccinia can. . .

DETDESC:

DETD(24)

In . . . preferred practice of the invention, virus stock of recombinant gp50:63 representing a titer of 8.1 Log 10 TCID<sub>50</sub>/ml is \*\*inactivated\*\* with BEI for 120 hours and used to inoculate pigs. Each animal received approximately one ml of the \*\*inactive\*\* virus preparation (containing 1-10 .mu.g of PRV protein) intramuscular. At three weeks a booster was given. Oil-lecithin was used as. . .

DETDESC:

4. 4,965,069, Oct. 23, 1990, Oxidized viruses or viral antigens and utilization for diagnostic prophylactic and/or therapeutic applications; Gerard A. Quash, et al., 424/208.1, 204.1, 209.1, 211.1, 212.1, 215.1, 216.1, 219.1, 225.1, 230.1, 231.1; 435/238 [IMAGE AVAILABLE]

US PAT NO: 4,965,069 [IMAGE AVAILABLE] L8: 4 of 5  
DRAWING DESC:

DRWD(3)

FIG. . . . in vivo administration of untreated parainfluenza virus (PIV) virus (A; control); PIV having an oxidized oligosaccharide moiety (B); PIV conventionally \*\*inactivated\*\* using beta-\*\*propiolactone\*\* (C); and PIV conventionally \*\*inactivated\*\* using beta-\*\*propiolactone\*\* and having an oxidized oligosaccharide moiety (D). Antibody titers were evaluated following 2 intraperitoneal injections of each of the PIV. . .

DETDESC:

DETD(26)

When . . . having an oxidized oligosaccharide moiety is used, it is necessary to use either an attenuated or avirulent virus or an \*\*inactivated\*\* virus. An \*\*inactivated\*\* virus is obtained by treatment of a virus with various chemicals such as formaldehyde; then an oligosaccharide is perturbed using any of the methods described above in Section 5.1. Alternatively, an \*\*inactivated\*\* virus having an oxidized oligosaccharide moiety is obtained by chemical oxidation of a virus, for example, using periodic acid as described in Section 5.1. Such attenuated or \*\*inactivated\*\* viruses having an oxidized oligosaccharide moiety induce antibodies that are more effective at neutralizing viral infections than conventionally attenuated or \*\*inactivated\*\* viruses.

DETDESC:

DETD(36)

The . . . not needed in this type of preparation because the object is not to stimulate an immune response, but rather to \*\*inactivate\*\* or bind a viral pathogen. Thus, any suitable pharmaceutical carrier can be used. Passive immunization using such preparations can be. . .

DETDESC:

DETD(41)

Specific . . . etc.; Parvoviridae such as parvoviruses, etc.; RNA viruses such as Togaviridae such as rubella, etc.; Paramyxoviridae such as measles, parainfluenza, \*\*respiratory\*\* \*\*syncytial\*\* virus, etc.; Flaviviridae such as dengue virus types 1-4, yellow fever virus, tick-borne fever viruses, etc.; Rhabdoviridae such as rabies, . . .

DETDESC:

DETD(92)

Infectivity of PIV \*\*inactivated\*\* by a conventional method using beta-\*\*propiolactone\*\* was also determined for comparison. Beta-\*\*propiolactone\*\* (Fluka) was added (final concentration 0.05 % v/v) to purified PIV (2 mg protein/ml) in 100 mM sodium borate-HCl, pH 9.0, and the mixture incubated for 2 hours 37.degree. C. At that time, fresh beta-\*\*propiolactone\*\* was added (final concentration 0.05 % v/v) and the mixture incubated for an additional 2 hours. The virus was then dialysed. . .

DETDESC:

DETD(93)

Another sample of purified PIV was first conventionally \*\*inactivated\*\* using beta-\*\*propiolactone\*\* and then

the oligosaccharide moiety oxidized as described above. The \*\*inactivated\*\* oxidized PIV was then extensively dialysed against PBS at 4.degree. C. (3 changes).

DETDESC:

DETD(95)

The . . . determined by estimation of the protein content following treatment. Yields were 50%, 75% and 52% of control respectively for oxidized, \*\*inactivated\*\* and \*\*inactivated\*\*-oxidized PIV. After adjusting all preparations to the same protein content, 50 ul aliquots of each were tested for infectivity as. . .

DETDESC:

DETD(98)

. . .

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#### INFECTIVITY OF PARAINFLUENZA VIRUS (PIV)

Infectious PIV Titer.sup.a

Treatment

Conventional

Sample	Oligosaccharide		
	Conventional	**Inactivation**	Conventional
No.	Control	Oxidation	**Inactivation** & Oxidation
1	> 10.sup.9	< 10	< 10
2	10.sup.5	< 10	< 10

.sup.a Infectious. . .

DETDESC:

DETD(99)

As . . . infectivity of the virus. In fact, oxidation of the carbohydrate moiety of the PIV virion was as effective as conventional \*\*inactivation\*\* using beta-\*\*propiolactone\*\*.

DETDESC:

DETD(102)

Sixty-six . . . four treatment groups: Group 1 (control) untreated PIV; Group 2, PIV having an oxidized oligosaccharide moiety; Group 3, PIV conventionally \*\*inactivated\*\* using beta-\*\*propiolactone\*\*; and Group 4, PIV conventionally \*\*inactivated\*\* using beta-\*\*propiolactone\*\* and having an oxidized oligosaccharide moiety. Animals in Series A, Series B and Series C received respectively-one (on day 0). . .

DETDESC:

DETD(108)

Results . . . when assayed by the oxidized oligosaccharide attached assay and conventional neutralization assays (FIG. 1A, B). In mice which received conventionally \*\*inactivated\*\* virus, there was a lag in the neutralizing antibody titer (FIG. 1C). In mice which received PIV which was both conventionally \*\*inactivated\*\* and in which the oligosaccharide moiety was oxidized as immunogen, the titer of neutralizing antibody obtained using virus neutralization assay. . .

DETDESC:

DETD(109)

From . . . in eliciting a significant neutralizing antibody response when administered in vivo. This response occurred earlier than that elicited by PIV \*\*inactivated\*\* by conventional methods using beta-\*\*propiolactone\*\*.

DETDESC:

DETD(117)

In animals which had been previously immunized with one, two or three intraperitoneal injections of either conventionally \*\*inactivated\*\* PIV or conventionally \*\*inactivated\*\* PIV having an oxidized carbohydrate moiety, no virus could be detected in lung homogenates at any time post-challenge with infectious virus. Thus it appears that PIV having an oxidized oligosaccharide moiety either with or without conventional \*\*inactivation\*\* is very effective in eliciting a protective immune response against infectious PIV.

DETDESC:

DETD(137)

Serum . . . and F. Barre-Sanussi of the Institut Pasteur, Paris. The samples had been incubated at 56.degree. C. for 30 minutes to \*\*inactivate\*\* any HIV virus present.

5. 4,962,091, Oct. 9, 1990, Controlled release of macromolecular polypeptides; Deborah A. Eppstein, et al., 424/85.2, 85.1, 85.4, 85.6, 130.1, 178.1, 184.1, 193.1, 499; 514/2, 21, 964 [IMAGE AVAILABLE]

US PAT NO: 4,962,091 [IMAGE AVAILABLE] L8: 5 of 5

DETDESC:

DETD(10)

The . . . by appropriate choice of the type and relative amount of comonomer used. Some illustrative examples of suitable comonomers include glycolide, .beta.-\*\*propiolactone\*\*, tetramethylglycolide, .beta.-butyrolactone, 4-butyrolactone, pivalolactone, and intermolecular cyclic esters of .alpha.-hydroxy butyric acid, .alpha.-hydroxyisobutyric acid, .alpha.-hydroxyvaleric acid, .alpha.-hydroxyisovaleric acid, .alpha.-hydroxy caproic. . .

DETDESC:

DETD(12)

The . . . acid units from which the preferred polymers are prepared may be the optically active (D- and L-) forms or optically \*\*inactive\*\* (DL-, racemic) forms. For example, lactic acid, whether it is the sole monomer, or a comonomer component, can be present. . .

DETDESC:

DETD(21)

Specific . . . virus II, malaria, pseudorabies, retroviruses, feline leukemia virus, bovine leukemia virus, transmissible gastroenteritis virus, infectious bovine rhinotracheitis, parainfluenza, influenza, rotaviruses, \*\*respiratory\*\* \*\*syncytial\*\* virus, varicella zoster virus, Epstein-Barr virus, pertussis, and anti-infective antibodies including monoclonal and polyclonal antibodies to gram negative bacteria, pseudomonas, . . .

=> s respiratory(w)syncytial/ti or respiratory(w)syncytial/ab                    11174 RESPIRATORY

    11 SYNCYTIAL/TI

    11 RESPIRATORY(W)SYNCYTIAL/TI

    11174 RESPIRATORY

    18 SYNCYTIAL/AB

    17 RESPIRATORY(W)SYNCYTIAL/AB

L9            17 RESPIRATORY(W)SYNCYTIAL/TI OR RESPIRATORY(W)SYNCYTIAL/AB

=> d l9 1-17 cit ab

1. 5,424,189, Jun. 13, 1995, Bovine \*\*respiratory\*\* \*\*syncytial\*\* virus detection and primers; Richard D. Oberst, et al., 435/6, 91.1, 91.2; 536/24.3, 24.32, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,424,189 [IMAGE AVAILABLE]                    L9: 1 of 17

ABSTRACT:

The use of specific primers and a probe in a reverse transcriptase- polymerase chain reaction provides a method for specifically identifying bovine \*\*respiratory\*\* \*\*syncytial\*\* virus in cattle.

2. 5,288,630, Feb. 22, 1994, Expression system for RSV glycoprotein F and G; Michael W. Wathen, 435/240.2, 69.7, 172.3, 252.3, 252.33, 254.2, 320.1; 536/23.4; 935/69, 70, 72 [IMAGE AVAILABLE]

US PAT NO: 5,288,630 [IMAGE AVAILABLE]                    L9: 2 of 17

ABSTRACT:

This invention encompasses DNA compositions encoding novel chimeric glycoproteins which are useful for preparing virus specific immune responses against human \*\*respiratory\*\* \*\*syncytial\*\* virus. The DNA compositions include structural genes coding for the glycoproteins and expression and replication plasmids containing the structural genes. Host cells transformed with the above DNA compositions, vaccines made from the glycoproteins and methods for protecting humans by inoculation with said vaccines are also part of this invention.

3. 5,256,668, Oct. 26, 1993, Aminopyrimidine derivatives as antiviral agents for \*\*respiratory\*\* \*\*syncytial\*\* virus; Kuo-Hom L. Hsu, et al., 514/269 [IMAGE AVAILABLE]

US PAT NO: 5,256,668 [IMAGE AVAILABLE]                    L9: 3 of 17

ABSTRACT:

Antiviral activity against \*\*respiratory\*\* \*\*syncytial\*\* virus has been found in some substituted 6-aminopyrimidines having the formula: ##STR1## wherein R.<sup>1</sup> is lower alkyl, preferably methyl or t-butyl, R.<sup>2</sup> is halogen or cyano, and R.<sup>3</sup> is C.<sub>1-6</sub> alkyl or -(CH<sub>2</sub>)<sub>n</sub> R.<sup>4</sup> where n is 1 or 2 and R.<sup>4</sup> is phenyl, phenyl substituted by lower alkoxy, lower alkyleneoxy, bromo, or 3,4-methylenedioxy; 3 or 4-pyridinyl, pyridinyl substituted by cyano or bromo, thienyl, or di-(C.<sub>1-6</sub> alkyl)amino.

4. 5,223,254, Jun. 29, 1993, \*\*Respiratory\*\* \*\*syncytial\*\* virus: vaccines; Peter R. Paradiso, et al., 424/186.1, 211.1; 514/2, 8, 12 [IMAGE AVAILABLE]

US PAT NO: 5,223,254 [IMAGE AVAILABLE]                    L9: 4 of 17

ABSTRACT:

Polypeptides, nucleotides, and compositions useful for preparing diagnostic reagents for and vaccines against human \*\*Respiratory\*\* \*\*Syncytial\*\* Virus are disclosed. The polypeptides include short polypeptides which

are related to a neutralizing and fusion epitope of the \*\*Respiratory\*\* \*\*Syncytial\*\* Virus fusion protein or a neutralizing epitope of the G protein.

5. 5,211,944, May 18, 1993, Proanthocyanidin polymers having antiviral activity and methods of obtaining same; Michael S. Tempesta, 424/78.08, 78.37, 195.1, 196.1 [IMAGE AVAILABLE]

US PAT NO: 5,211,944 [IMAGE AVAILABLE] L9: 5 of 17

ABSTRACT:

The present invention provides for proanthocyanidin polymers with significant antiviral activity. The proanthocyanidin polymers can be chemically synthesized or can be isolated from a Croton or a Calophyllum plant species. The present invention encompasses methods of using proanthocyanidin polymers in treating warm-blooded animals, including humans, infected with paramyxoviridae such as \*\*respiratory\*\* \*\*syncytial\*\* virus, orthomyxoviridae such as influenza A, B and C, and herpes viruses such as Herpes Simplex virus.

6. 5,194,595, Mar. 16, 1993, Chimeric glycoproteins containing immunogenic segments of the glycoproteins of human \*\*respiratory\*\* \*\*syncytial\*\* virus; Michael W. Wathen, 530/395; 424/186.1, 211.1; 435/69.7, 172.3 [IMAGE AVAILABLE]

US PAT NO: 5,194,595 [IMAGE AVAILABLE] L9: 6 of 17

ABSTRACT:

This invention encompasses DNA compositions encoding novel chimeric glycoproteins which are useful for preparing virus specific immune responses against human \*\*respiratory\*\* \*\*syncytial\*\* virus. The DNA compositions include structural genes coding for the glycoproteins and expression and replication plasmids containing the structural genes. Host cells transformed with the above DNA compositions, vaccines made from the glycoproteins and methods for protecting humans by inoculation with said vaccines are also part of this invention.

7. 5,149,650, Sep. 22, 1992, Vaccines for human respiratory virus; Gail W. Wertz, et al., 435/243 [IMAGE AVAILABLE]

US PAT NO: 5,149,650 [IMAGE AVAILABLE] L9: 7 of 17

ABSTRACT:

This invention discloses compositions of DNA and proteins that are useful for preparing vaccines against human \*\*respiratory\*\* \*\*syncytial\*\* virus [HRSV]. The DNA compositions include structural genes coding for native structural viral proteins and immunogenic fragments of these proteins. Host cells transformed with the above DNA compositions are also disclosed. Vaccines made from the native structural viral proteins or immunogenic fragments are also disclosed as well as methods for protecting humans by inoculation with these vaccines.

8. 5,071,758, Dec. 10, 1991, Production of cell strains capable of propagating \*\*respiratory\*\* \*\*syncytial\*\* virus, compositions containing such virus and their use in diagnosis of \*\*respiratory\*\* \*\*syncytial\*\* virus infection; Edward J. Stott, et al., 435/240.2; 424/201.1, 211.1; 435/29, 41, 235.1; 436/518, 519, 811 [IMAGE AVAILABLE]

US PAT NO: 5,071,758 [IMAGE AVAILABLE] L9: 8 of 17

ABSTRACT:

Antigens specific to \*\*respiratory\*\* \*\*syncytial\*\* virus are produced on the surface of cells by:

- (1) culturing in vitro cells derived from a human or animal mucosa, (2) inoculating the cultured cells with \*\*respiratory\*\* \*\*syncytial\*\* virus, and
- (3) selecting virally infected cells from the culture.

The resulting cells or the viral antigen(s) when partially or completely isolated from the cells have immunological and diagnostic uses in respect of infection by \*\*respiratory\*\* \*\*syncytial\*\* virus and may be used to isolate viral antibodies. A specific cell strain NM7 produced by this method from bovine nasal mucosal cells has \*\*respiratory\*\* \*\*syncytial\*\* virus antigens on its surface and its corresponding, uninfected cell strain

NM5 can be infected similarly.

9. 4,800,078, Jan. 24, 1989, Immunotherapeutic method of treating respiratory disease by intranasal administration of IgB; Gregory Prince, et al., 424/159.1, 177.1 [IMAGE AVAILABLE]

US PAT NO: 4,800,078 [IMAGE AVAILABLE]

L9: 9 of 17

ABSTRACT:

A new immunotherapeutic method of treating lower respiratory tract infection caused by \*\*respiratory\*\* \*\*syncytial\*\* virus (RSV) is disclosed. The method employs topical application of RSV antibodies into the lower respiratory tract. The new treatment modality is more effective and rapid than the conventional therapy.

10. 4,717,766, Jan. 5, 1988, Method of preparing high titer anti-\*\*respiratory\*\* \*\*syncytial\*\* virus intravenous immune globulin; Milton B. Dobkin, 530/389.4; 424/159.1, 177.1 [IMAGE AVAILABLE]

US PAT NO: 4,717,766 [IMAGE AVAILABLE]

L9: 10 of 17

ABSTRACT:

Normal plasma from donors who have not necessarily been vaccinated with a \*\*respiratory\*\* \*\*syncytial\*\* virus vaccine can be screened for higher than normal titers of naturally occurring antibody to \*\*respiratory\*\* \*\*syncytial\*\* virus (e.g. minimum ELISA titer of at least 1:110,000). Those plasmas with high titers of such antibody can be pooled and fractionated to give hyperimmune globulin. The product may be treated to render it suitable for intravenous injection. Patients with \*\*respiratory\*\* \*\*syncytial\*\* virus infection or at risk of such infection, may receive the present product to raise serum antibody titers to \*\*respiratory\*\* \*\*syncytial\*\* virus. Resultant product has an ELISA anti-RSV titer of at least about 1:250,000.

11. 4,659,563, Apr. 21, 1987, High titer anti-\*\*respiratory\*\* \*\*syncytial\*\* virus intravenous immune globulin; Milton B. Dobkin, 424/159.1, 177.1; 530/389.4, 390.5 [IMAGE AVAILABLE]

US PAT NO: 4,659,563 [IMAGE AVAILABLE]

L9: 11 of 17

ABSTRACT:

Normal plasma from donors who have not necessarily been vaccinated with a \*\*respiratory\*\* \*\*syncytial\*\* virus vaccine can be screened for higher than normal titers of naturally occurring antibody to \*\*respiratory\*\* \*\*syncytial\*\* virus (e.g. minimum ELISA titer of at least 1:110,000). Those plasmas with high titers of such antibody can be pooled and fractionated to give hyperimmune globulin. The product may be treated to render it suitable for intravenous injection. Patients with \*\*respiratory\*\* \*\*syncytial\*\* virus infection or at risk of such infection, may receive the present product to raise serum antibody titers to \*\*respiratory\*\* \*\*syncytial\*\* virus. Resultant product has an ELISA anti-RSV titer of at least about 1:250,000.

12. 4,619,942, Oct. 28, 1986, Inhibition of \*\*Respiratory\*\* \*\*Syncytial\*\* virus-induced cell fusion by amidino compounds; Richard R. Tidwell, et al., 514/415, 394, 636 [IMAGE AVAILABLE]

US PAT NO: 4,619,942 [IMAGE AVAILABLE]

L9: 12 of 17

ABSTRACT:

A number of aromatic mono- and bis-amidines are capable of blocking cell fusion induced by \*\*Respiratory\*\* \*\*Syncytial\*\* (RS) virus. Suitable amidino compounds include those selected from the group consisting of 1-4-di(4-amidinophenoxy)-2-butanol; bis(5-amidino-2-benzimidazolyl)methane; 1,2-bis(5-amidino-2-benzimidazolyl)ethane; 5-amidino-indole; 5-amidinobenzimidazole, 5-amidino-1-methylindole and 5-amidino-1-(4-amidinobenzyl)indole. The most powerful of the compounds, bis(5-amidino-2-benzimidazolyl)methane (BABIM), is able to achieve complete suppression of syncytium formation at a concentration of 1  $\mu$ M. Inhibition occurs in RS virus-infected Hep-2 cells as well as CV-1 cells. BABIM also causes a significant retardation of RS virus penetration, but does not interfere with adsorption. Addition of the amidines after the penetration of RS virus does not affect single cycle yields. The compounds may be used in the prophylactic control of RS virus in man.

13. 4,517,304, May 14, 1985, Production of viral antigens; Edward J. Stott, et al., 424/211.1; 435/5, 29, 41, 240.2, 240.25; 436/518, 811 [IMAGE AVAILABLE]

US PAT NO: 4,517,304 [IMAGE AVAILABLE]

L9: 13 of 17

ABSTRACT:

Antigens specific to \*\*respiratory\*\* \*\*syncytial\*\* virus are produced on the surface of cells by:

(1) culturing in vitro cells derived from a human or animal mucosa, (2) inoculating the cultured cells with \*\*respiratory\*\* \*\*syncytial\*\* virus, and

(3) selecting virally infected cells from the culture.

The resulting cells or the viral antigen(s) when partially or completely isolated from the cells have immunological and diagnostic uses in respect of infection by \*\*respiratory\*\* \*\*syncytial\*\* virus and may be used to isolate viral antibodies. A specific cell strain NM7 produced by this method from bovine nasal mucosal cells has \*\*respiratory\*\* \*\*syncytial\*\* virus antigens on its surface and its corresponding, uninfected cell strain NM5 can be infected similarly.

14. 4,397,863, Aug. 9, 1983, Inhibition of \*\*respiratory\*\* \*\*syncytial\*\* virus-induced cell fusion by amidino compounds; Richard R. Tidwell, et al., 514/415 [IMAGE AVAILABLE]

US PAT NO: 4,397,863 [IMAGE AVAILABLE]

L9: 14 of 17

ABSTRACT:

A number of aromatic mono- and bis-amidines are capable of blocking cell fusion induced by \*\*Respiratory\*\* \*\*Syncytial\*\* (RS) virus. Suitable amidino compounds include those selected from the group consisting of 1-4-di(4-amidinophenoxy)-2-butanol; bis(5-amidino-2-benzimidazolyl)methane; 1,2-bis(5-amidino-2-benzimidazolyl)ethane; 5-amidino-indole; 5-amidinobenzimidazole, 5-amidino-1-methylindole and 5-amidino-1-(4-amidinobenzyl)indole. The most powerful of the compounds, bis(5-amidino-2-benzimidazolyl)methane (BABIM), is able to achieve complete suppression of syncytium formation at a concentration of 1 .mu.M. Inhibition occurs in RS virus-infected Hep-2 cells as well as CV-1 cells. BABIM also causes a significant retardation of RS virus penetration, but does not interfere with adsorption. Addition of the amidines after the penetration of RS virus does not affect single cycle yields. The compounds may be used in the prophylactic control of RS virus in man.

15. 4,324,794, Apr. 13, 1982, Inhibition of \*\*respiratory\*\* \*\*syncytial\*\* virus-induced cell fusion by amidino compounds; Richard R. Tidwell, et al., 514/387; 435/172.2; 935/93, 95 [IMAGE AVAILABLE]

US PAT NO: 4,324,794 [IMAGE AVAILABLE]

L9: 15 of 17

ABSTRACT:

A number of aromatic mono- and bis-amidines are capable of blocking cell fusion induced by \*\*Respiratory\*\* \*\*Syncytial\*\* (RS) virus. Suitable amidino compounds include those selected from the group consisting of 1-4-di(4-amidino-phenoxy)-2-butanol; bis(5-amidino-2-benzimidazolyl)methane; 1,2-bis(5-amidino-2-benzimidazolyl)ethane; 5-amidino-indole; 5-amidinobenzimidazole, 5-amidino-1-methylindole and 5-amidino-1-(4-amidinobenzyl)indole. The most powerful of the compounds, bis(5-amidino-2-benzimidazolyl)methane (BABIM), is able to achieve complete suppression of syncytium formation at a concentration of 1 .mu.M. Inhibition occurs in RS virus-infected Hep-2 cells as well as CV-1 cells. BABIM also causes a significant retardation of RS virus penetration, but does not interfere with adsorption. Addition of the amidines after the penetration of RS virus does not affect single cycle yields. The compounds may be used in the prophylactic control of RS virus in man.

16. 4,145,252, Mar. 20, 1979, \*\*Respiratory\*\* \*\*syncytial\*\* vaccine; Eugene B. Buynak, et al., 435/237 [IMAGE AVAILABLE]

US PAT NO: 4,145,252 [IMAGE AVAILABLE]

L9: 16 of 17

ABSTRACT:

By serially passaging virulent \*\*respiratory\*\* \*\*syncytial\*\* virus in human diploid lung fibroblasts, a non-pathogenic but antigenic live \*\*respiratory\*\* \*\*syncytial\*\* virus is produced. This virus is useful in preparing a live virus vaccine.

17. 4,122,167, Oct. 24, 1978, Respiratory syncytial vaccine; Eugene B. Buynak, et al., 424/211.1, 278.1;

435/237 [IMAGE AVAILABLE]

US PAT NO: 4,122,167 [IMAGE AVAILABLE]

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